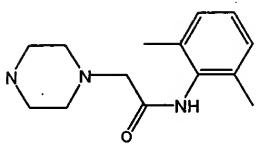
REMARKS

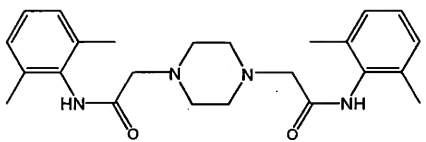
Claims 1-6 are pending. Claim 3 has been amended to recite that the ratio in step a) of piperazine to N-haloacetyl-2,6-xylidine is about 3/1. Claim 5 has been amended to recite that the separation method in step f) is filtration.

Claims 1-6 stand rejected under 35 U.S.C. § 103 as allegedly obvious over U.S. 4,123,530 (Corvi-Mora). The Applicants disagree and request withdrawal of the rejection and allowance of the pending claims.

The instant claims are directed to novel processes for the preparation of N-(2,6-dimethyl-phenyl)-2-piperazin-1-yl-acetamide:



As detailed in the specification, processes for the preparation of N-(2,6-dimethyl-phenyl)-2-piperazin-1-yl-acetamide that are described in the art are unsatisfactory because of the formation of an undesired adduct, Formula IV:



"Several process have been developed in order to reduce the amount of adduct; . . . [h]owever, all of the known methods have the disadvantage that they are not well suit[ed] for the exploitation of the reaction on an industrial scale, in particular for a process that produces a

dispersion or slurry from which the solid part can be obtained by industrial separation methods, in particular by filtration." Specification at page 1, lines 18-26.

In contrast to the methods described in the art, the claimed process is suitable for industrial scale reactors. In addition, the claimed process enables the undesired adduct to be removed by filtration and also provides the desired compound in solid form. Among other things, the claimed process requires:

a) reacting piperazine with N-haloacetyl-2,6-xylidine in a molar ratio of piperazine to N-haloacetyl-2,6-xylidine between about 1/1 and about 6/1 in an aqueous solvent in which has been dissolved in an about equimolar amount of HCl relative to the molar amount of piperazine;

b) separating the solid formed in step a) from the reaction mixture by filtration to create a filtrate;

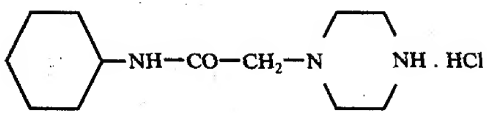
c) neutralizing the filtrate;

d) extracting the filtrate with a solvent which is not or only slightly miscible with the aqueous solvent mentioned in step a);

e) crystallizing the N-(2,6-dimethyl-phenyl)-2-piperazin-1-yl-acetamide from the solvent mentioned in step d); and

f) separating the solid obtained in step e) from the solvent mentioned in step d).

Corvi-Mora, as the Office acknowledges, only expressly describes the preparation of N-(cyclohexyl)-2-piperazin-1-yl-acetamide:



The preparation of N-(2,6-dimethyl-phenyl)-2-piperazin-1-yl-acetamide is not expressly described. In addition, Corvi-Mora fails to describe that any undesirable adducts form during the preparation of N-(cyclohexyl)-2-piperazin-1-yl-acetamide or that any special steps, reaction conditions, precautions, etc. are necessary to avoid adduct formation.

The methods described in Corvi-Mora (Examples 1-5) are all similar, requiring the combination of combining piperazine hydrochloride with N-(chloracetyl)-cyclohexylamine in water, heating the mixture at reflux, cooling the reaction mixture, making the mixture alkaline by the addition of NaOH, and extracting the aqueous phase with chloroform. The chloroform extract is then washed with water, dried, filtered, and evaporated. The resulting residue is then distilled under reduced pressure. Alternatively, the reaction can be carried out in organic solvents, for example chloroform or benzene.

Among other things, Corvi-Mora fails to describe filtration step b), crystallization step e), or separation step f) of independent claims 1 and 6. Moreover, these steps could not been discerned by the skilled person because Corvi-Mora fails to describe the formation of any solid during the reaction and also teaches that the product should be distilled, not recrystallized. For at least these reasons, the claimed methods are nonobvious over the art and the rejection should be withdrawn.

The Applicants assert that claims 1-6 are in condition for allowance. An early notice to that effect is, therefore, earnestly solicited.

Date: September 22, 2010

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